

Attorney Docket No.: P-408 (TI-0013)  
Inventor: Taylor et al.  
Serial No.: 09/802,466  
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#### **REMARKS**

Claims 1, 2, 4-11, 21, 26-28, and 33 are pending in the instant application. Claims 1, 2, 4-11, 21, 26-28, and 33 have been rejected. Claims 7, 10, 26 and 28 have been amended. Claims 5 and 33 have been canceled. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

#### **I. Claim Objections**

The Examiner has objected to claim 5 under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 26 is objected to because the limitation reciting that the RNA molecule is separated from the agent capable of catalyzing RNA degradation by MIPC is redundant in that this limitation is also found in claim 1 upon which claim 26 is dependent.

Applicants have canceled claim 5 and amended claim 26 to remove reference to the separation of RNA from the RNA degrading agent by MIPC. Withdrawal of these objections is respectfully requested.

#### **II. Rejection of Claims Under 35 U.S.C. §112**

Claim 27 has been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner suggests that the recitation of a method of stabilizing an RNA molecule against degradation performed under conditions that are free of multivalent cations capable of interfering with polynucleotide separation is not

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sufficiently disclosed in the instant application. It is suggested the disclosure in providing a single condition which is not accompanied by a disclosure as to the relative properties of preparing the medium by acid wash or by addition of cation binding reagents is insufficient for one of skill in the art to envision such conditions. The Examiner suggests that given the diversity of conditions that the invention must be empirically determined and in an unpredictable art the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of the claimed genus. Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully disagree with the Examiner's suggestion that one of skill would have insufficient guidance in preparing separation medium which is substantially free of multivalent cations as the Examiner has cited multiple references which specifically disclose the removal of multivalent cations from separation media (e.g., U.S. Patent No. 5,972,222). It was well-known at the time of filing that agents such as EDTA or EGTA bind multivalent actions. Further, Examples 8 and 9 (page 45, lines 1-21) of the instant application expressly provide guidance in how to prepare an acid washed separation medium and the use of a cation-binding reagent such as EDTA, respectively. Moreover, the use of a cation exchange resin in sodium or hydrogen form is disclosed for removing multivalent metal cations by conventional ion exchange. See page 14, lines 12-14 of the instant application. Given the sufficient guidance provided by the instant application and what was well-established in the art at the time of filing, Applicants believe that the written

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description requirement has been met. It is therefore respectfully requested that this rejection be withdrawn.

Claims 26 and 28 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, claim 26 is rejected in its recitation of the limitations "mRNA degradation" and "the separation" as there is insufficient antecedent basis for these limitations in claim 1. Claim 28 is likewise rejected for reciting the limitation "mRNA degradation" without an antecedent basis.

As the limitation "mRNA *degradation*" was not identified in either of claim 26 or 28, Applicants are assuming that the Examiner meant the limitation of "mRNA *denaturation*". Thus, Applicants have amended claims 26 and 28 to recite that "RNA elution is achieved by conducting the separation at a temperature sufficient to denature the RNA molecule..." Support for this amendment can be found at page 25, lines 23-25 of the specification. Further, Applicants respectfully disagree with the Examiner's suggestion that there is insufficient antecedent basis for the term "the separation" in claim 26 as claim 1 recites in step b) that "where the elution is conducted under conditions that result in a separation of the RNA molecule from the agent capable of catalyzing the degradation of RNA ...". It is therefore respectfully requested that these rejections be withdrawn.

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### III. Rejection of Claims Under 35 U.S.C. §102

Claim 33 is rejected under 35 U.S.C. 102(b) as being anticipated by Gjerde (WO 98/56798). The rejection of claim 33 under 35 U.S.C. 102(e) and 102(a), as being anticipated by Gjerde et al. (U.S. Patent Nos. 5,972,222) and Gjerde et al. (U.S. Patent No. 5,986,085) has been maintained.

To facilitate prosecution of this application, Applicants have canceled claim 33. Withdrawal of these rejections is therefore respectfully requested and .

Claims 1, 2, 4-11, 21, 26-28 and 33 are rejected under 35 U.S.C. §102(e) as being anticipated by Gerde et al. (U.S. Patent Application No. 20030165941). The rejection of claims 7-10, 26, 28 and 33 under 35 U.S.C. 102(a) as being anticipated by Oefner (U.S. Patent No. 6,453,244) has also been maintained. Applicants respectfully traverse these rejections under 35 U.S.C. 102 as they apply to claims 1, 2, 4-11, 21, and 26-28.

Applicants respectfully disagree with the Examiner's analysis and conclusions regarding the cited references. While the cited references read on the separation of a mixture of polynucleotides such as DNA and RNA, each of these references is silent to the separation of a polynucleotide molecule from any other type of macromolecule, e.g., an RNA degrading agent, thereby stabilizing the RNA molecule against degradation. As is well-known to one of skill in the art, chromatographic conditions suitable for separating a protein from other proteins or a polynucleotide from other polynucleotides may not be sufficient to separate, e.g., a protein from a polynucleotide, as any particular protein may have the same binding and elution characteristics as any particular polynucleotide. The present

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invention is based on unexpected finding that conditions which are suitable for separating polynucleotides from each other are also generally suitable for separating an RNA molecule from an agent capable of catalyzing the degradation of RNA. To anticipate a claim, the reference must teach every element of the claim. See MPEP §2131. Because the cited references are silent as to the separation of an RNA molecule from an agent capable of catalyzing the degradation of RNA thereby stabilizing the RNA molecule against degradation, these references can not anticipate the subject matter of claims 1, 2, 4-11, 21, and 26-28. Withdrawal of these rejections is therefore respectfully requested.

The rejection of claims 7-10 and 33 under 35 U.S.C. 102(b) as being anticipated by Joachimiak (ABRF News, December 1992) has been maintained. The Examiner suggests that because the limitations of claim 5 were not incorporated into claims 7-10 and 33 that these claims remain rejected in view of Joachimiak.

In an effort to advance the prosecution of the present invention, claims 7-10 have been amended to recite that the separation of the RNA molecule from the agent capable of catalyzing the degradation of RNA is conducted by Matched Ion Polynucleotide Chromatography. Support for this amendment is found throughout the specification and at claim 5 as filed. It has been indicated that the limitation of claim 5 is allowable in view of the Joachimiak reference. Withdrawal of this rejection is therefore respectfully requested.

#### **IV. Rejection of Claims Under 35 U.S.C. §103**

Claims 1-2, 4-6 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oefner (U.S. Patent No. 6,453,244) in

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view of Petro et al. (U.S. Patent No. 6,260,407). Claims 11 and 27 also stand rejected under 35 U.S.C. 103(a) as being unpatentable over Oefner in view of Petro et al. further in view of Sheridan and Sheridan ((1989) *Scientist* 3(4)23).

The Examiner suggests that Oefner teaches elution of RNA with a mobile phase containing an ion-pairing reagent and organic solvent under denaturing conditions such as heat or chemicals. The solid support is comprised of silica and the mobile phase is comprised of TEAA and acetonitrile. Denaturing conditions include temperatures up to 70°C to 80°C. The separation media has an average diameter of 1-100 microns, the concentration of TEAA is about 0.05 to 1.0 Molar and about 25% acetonitrile. The Examiner suggests that while this reference does not teach this invention can be used in the separation of RNA and the procedure can be used for large numbers of samples to be analyzed. The Examiner further suggests that while Oefner fails to teach a mobile phase control means that is controlled by a computer that Petro et al. provide the motivation to use computer controls to receive the expected benefit of generating a high-throughput automated sampling system. It is further suggested that while Oefner and Petro et al. fail to teach that conditions of separation are free of multivalent cations that Sheridan and Sheridan teach a Metal-Free column system for use in chromatography in which the recovery of biopolymers is improved. Applicants respectfully traverse this rejection.

To the extent that the primary reference of Oefner does not anticipate the present invention as discussed *supra*, neither does it make the instant invention obvious either alone or in combination with Petro et al. or Sheridan and Sheridan as none of

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these references teach or suggest the separation of an RNA molecule from any other molecule, in particular an agent capable of catalyzing the degradation of RNA. It is therefore respectfully requested that these rejections be withdrawn.

**V. Conclusion**

The Applicants believe that the foregoing comprises a full and complete response to the Advisory Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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